REMARKS

Claims 1, 3, 5, 7, 9, 11 and 20 are amended herein. Claims 13-19 are canceled, and new Claims 23-36 are added herein. Support for the amendments to Claims 1, 3, 5, 7, 9, 11 and 20, can be found throughout the specification, for example, on page 6, lines 16-24, and page 8, lines 7-29. Support for new claims 23-36 is found in the claims as originally filed and in the specification, for example, at page 4, lines 14-28, page 6, lines 16-24, page 8, lines 7-29, and Figure 1-3. The amendments to the claims and new claims do not add new matter.

Claims 1-12 and 20-36 are presented for examination.

Rejections Under 35 U.S.C §112, Second Paragraph

Claims 1, 3, 5, 7, 9 and 11 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter, which applicant regards as the invention. The Office Action states that the term "said degenerate or universal base" lacks antecedent basis because there can be multiple mismatches. Claims 1, 3, 5, 7, 9 and 11 have been amended to more definitely and clearly recite that "wherein one or more non-naturally occurring base is positioned in said antisense oligonucleotide to align with a nucleotide mismatch position in the target regions of the RNA molecules." The claims now clearly indicate that the mismatches of interest are within the target regions of the RNA molecules and that one or more non-naturally occurring base is positioned to align with one or more nucleotide mismatch. Applicants respectfully submit that this language of the claims is not indefinite, and, accordingly Applicants request the withdrawal of this rejection.

Claims 1-12 and 20-22 stand rejected under 35 U.S.C § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter, which applicant regards as the invention. The Office Action states that the term "said nucleotide mismatch" lacks antecedent basis because there can be multiple mismatches. In view of the above-discussed amendment to Claims 1, 3, 5, 7, 9 and 11, Applicants submit that reference to a mismatch position in the target region of the RNA molecule is presently not indefinite. Accordingly Applicants respectfully request the withdrawal of this rejection.

Claims 1-12 and 20-22 also stand rejected under 35 U.S.C § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter, which applicant regards as the invention because the claim as previously written allegedly read on any antisense oligonucleotide that hybridized to two RNA molecules, and the location of the mismatch was not required to be in the location of the mRNA that is hybridized by the claimed antisense oligonucleotide. As discussed above, the claims now clearly indicate that the mismatches of interest are within the target regions of the RNA molecules and that one or more non-naturally occurring base is positioned to align with one or more nucleotide mismatch. Accordingly, Applicants respectfully submit that the language of the claims is not presently indefinite, and Applicants request the withdrawal of this rejection.

Rejection Under 35 U.S.C §112, First Paragraph

Claims 1-12 stand rejected under 35 U.S.C § 112, first paragraph, as containing subject matter, which was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

To satisfy the written description requirement, a patent application must describe the invention in sufficient detail that one of skill in the relevant art could conclude that the inventor was in possession of the claimed invention at the time the application was filed. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991). According to the Federal Circuit, it is clear that Applicants need not precisely recite each and every element of a claim limitation in the specification in order to satisfy the written description requirement. *See Union Oil of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989 (Fed. Cir. 2000). Information that is well known in the art need not be described in detail in the specification, and is preferably omitted. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986).

The Office Action states that the specification does not disclose a specific structure that corresponds with the function of being antisense, as claimed.

Applicants respectfully traverse this rejection.

In view of the amendment to the claims, Applicants address this rejection first as it applies to Claims 1-6 as amended, and second as it applies to Claims 7-12 as amended.

Claims 1-6

Claims 1-6, as amended, are directed to improved antisense oligonucleotides, where the improvement includes one or more base of the antisense oligonucleotide being a non-naturally occurring base selected from the group consisting of a degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. As such, Claims 1-6 acknowledge that antisense oligonucleotides are known in the art, and indicate that the claimed improvements include the recited modification(s) to said antisense oligonucleotides. Thus, the claims recite antisense oligonucleotide structures, which are known in the art, as modified by the recited improvements. That is, one skilled in the art readily appreciates the structure of antisense oligonucleotides in the prior art and the improvements made thereto as described in the specification and recited in the claims. Accordingly, Applicants respectfully submit that they were in possession of the invention and have met the requirements of 35 U.S.C § 112, first paragraph.

Additionally the claims recite that the antisense oligonucleotide includes one or more non-naturally occurring base selected from the group consisting of a degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. These elements of the claims are chemical structures that are provided for use with antisense oligonucleotides in the specification (see, e.g., page 4, lines 18-31, page 6, lines 16-24, and page 8, lines 7-29). Thus, these elements are described in the specification, and the requirements under 35 U.S.C § 112, first paragraph have been met.

Further, Claim 5 recites a RNase H recruiting region, which is also disclosed in the specification in terms of its structural components and function, for example, at page 7, lines 1-4. Claim 3 recites a RNase recruiting region, which is supported by numerous RNase recruiting regions disclosed in the specification, for example, RNase H recruiting regions (see above), RNase L recruiting regions and RNase P recruiting regions (see, e.g., page 7, lines 10-18).

In view of the above, Applicants submit that Claims 1-6, as written, fully comply with the written description requirement because the claimed subject matter was either known in the art or was described in the specification in such a way as to convey to one skilled in the art that the inventors had possession of the claimed invention. Accordingly, Applicants respectfully request that the rejection of Claims 1-6 under 35 U.S.C § 112, first paragraph, be removed.

Claims 7-12

Claims 7-12, as amended, are also fully described in the specification. Guidance to specific RNase recruiting regions and targeting regions are provided in the specification and one of skill in the art readily appreciates the structural elements that are recited in the claims. For example, Claim 7, as amended, is directed to an antisense oligonucleotide comprising an RNA targeting region and a RNase L-recruiting region comprising a 2'-5' adenosine oligomer, wherein the RNA targeting region of said antisense oligonucleotide comprises one or more non-naturally occurring base selected from the group consisting of degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. The specification provides specific guidance on the structure of a RNase L-recruiting region. For example, the specification at page 3, lines 1-5, page 7, lines 10-13, and page 10, line 10, through page 11, line 3, teaches specific structural details for region that recruits RNase L. The specification also cites U.S. Patent No. 5,583,032 for structure of regions that recruit RNase L. Furthermore, Claim 7 recites that the RNase L-recruiting region comprises a 2'-5' adenosine oligomer. Accordingly, the specification teaches, and Claim 7 recites, specific structure that corresponds with the function of being a RNase L-recruiting region. As such, Claim 7 is sufficiently described by the specification.

Claim 9, as amended, is directed to an antisense oligonucleotide comprising an RNA targeting region and a RNase P-recruiting region, wherein the RNA targeting region of said antisense oligonucleotide comprises one or more non-naturally occurring base selected from the group consisting of degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. The specification provides specific guidance on the structure of a RNase P-recruiting region. For example, the specification at page 7, lines 14-18, page 10, line 10, through page 11, line 3, and SEQ ID NO:11, teaches specific structural details for regions that recruit RNase P. The specification also cites U.S. Patent No. 5,877,162 and the publication by Ma et al.

(Antisense Nucl. Acid Drug Dev. 8:415-426, 1998) for structure of regions that recruit RNase P. Accordingly, those skilled in the art readily appreciate the specific structures that correspond with the function of being a RNase P-recruiting region. As such, Claim 9 is sufficiently described by the specification.

Claim 11, as amended, is directed to a ribozyme comprising an RNA targeting region, which comprises one or more non-naturally occurring base selected from the group consisting of degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. The specification provides specific guidance on the structure of a ribozyme. For example, the specification at page 9, line 31, through page 10, line 6, teaches a specific type of ribozyme, and references the publication by Benseler et al. (J. Am. Chem. Soc. 115:8483-8484, 1993) for additional ribozyme structural details. Accordingly, the specification teaches and points to a reference that teaches specific structural details that correspond with the function of being a ribozyme. As such, Claim 11 is sufficiently described by the specification.

In view of the above, Applicants submit that Claims 7-12, as written, fully comply with the written description requirement because the claimed subject matter was described in the specification in such a way as to convey to one skilled in the art that the inventors had possession of the claimed invention. Accordingly, Applicants respectfully request that the rejection of Claims 7-12 under 35 U.S.C § 112, first paragraph, be removed.

Rejections Under 35 U.S.C. § 102

Claims 1-8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cook et al., U.S. Patent No. 5,623,065. Claims 1, 2 and 4-8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Torrence et al., U.S. Patent No. 5,583,032. Claims 1, 2, 7, 8, 11 and 12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Stinchcomb et al., U.S. Patent No. 5,646,042. Claims 1-6 are rejected under 35 U.S.C. § 102(e) as being anticipated by Bennett et al., U.S. Patent No. 6,172,216. The Office Action states that these patents disclose all elements of the respective rejected claims.

Applicants respectfully traverse this rejection.

A reference must teach each and every element to anticipate a claim under 35 U.S.C. § 102. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. ...There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

Independent claims 1, 3, 5, 7 and 11 recite that the claimed antisense oligonucleotide or ribozyme contains one or more non-naturally occurring base selected from the group consisting of a degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. None of the cited references disclose an antisense oligonucleotide or ribozyme containing one or more non-naturally occurring base selected from the group consisting of a degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. Accordingly, none of the cited references anticipate any of independent claims 1, 3, 5, 7 and 11, or claims dependent therefrom.

Rejection Under 35 U.S.C. § 103

Claims 7-12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Werther et al. (US Patent 5,929,040) in view of Bennett et al., Torrence et al., and Krupp (Biochemie 75:135-139 1993).

Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must teach or suggest all the claim elements. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Applicants respectfully submit that the cited art does not render Claims 7-12 *prima facie* obvious because the cited art, alone or in any combination, fails to teach or suggest all claim elements. Independent claims 7, 9 and 11 recite that the claimed antisense oligonucleotide or ribozyme contains one or more non-naturally occurring base selected from the group consisting of a degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. None

of the cited references, alone or combined, teach or suggest an antisense oligonucleotide or ribozyme containing one or more non-naturally occurring base selected from the group consisting of a degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine. Accordingly, no combination of the cited references teaches or suggests all elements of independent claims 7, 9 and 11, or claims dependent therefrom. In view of the foregoing, Applicants respectfully request the withdrawal of this rejection and allowance of the pending claims.

CONCLUSION

In view of the above, Applicants respectfully submit that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11 1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 16-Aug-05

By: _____

Kerry Taylor
Registration No. 43,947
Attorney of Record
Customer No. 20,995
(619) 235-8550

1866580\081505